Peripheral Sweat Gland Function Improves With Humid Heat Acclimation

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Peripheral sweat gland function is improved with humid heat acclimation

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ABSTRACT

1. The purpose of this study was to determine if humid heat acclimation improves thermoregulatory function at the level of the eccrine sweat gland.
2. Mean rectal temperature and heart rate were significantly ($p<0.05$) reduced by 0.5 °C and 17 bpm, respectively, during an 8-day heat acclimation protocol in 13 male subjects.
3. Whole-body sweat rate was also significantly increased 20% during the same time period. The most important new finding was that humid heat acclimation produced a significant 63% increase in pilocarpine-induced sweat rate. These results strongly suggest that heat acclimation improves sweat gland function via a peripheral mechanism.

1. Introduction

It is well documented that whole-body sweat rate (WBSR) is increased following heat acclimation (HA) (Garden et al., 1966; Mitchell et al., 1976; Patterson et al., 2004; Strydom et al., 1966); however the mechanism is not completely understood. Specifically, heat acclimation has been shown to lower the core-temperature threshold at which sweat production is initiated (Armstrong and Kenney, 1993; Nadel et al., 1974; Roberts et al., 1977; Wyndham, 1967; Yamazaki and Hamasaki, 2003). This has been interpreted (Nadel et al., 1974) to indicate that HA primarily increases WBSR via modification of the central nervous system (i.e., a central mechanism). On the contrary, other studies (Chen and Elizondo, 1974; Collins et al., 1966; Inoue et al., 1999; Sato et al., 1990) have found increased sweat production following HA via direct stimulation of the eccrine glands using electrical or pharmacological techniques. Such results suggest that the change in WBSR seen following HA must be at least partly due to modifications in the sweat glands (i.e., a peripheral mechanism). However, a close examination of the four published studies (Chen and Elizondo, 1974; Collins et al., 1966; Inoue et al., 1999; Sato et al., 1990) that have used electrical or pharmacological stimulation to directly measure the effect of HA on peripheral sweat gland function reveals that they all have methodological concerns, which makes interpretation of the results difficult. For example, the classic study by Collins et al. (1966) reported that intradermal methacholine-induced sweat production increased 125% following 10 days of HA. However, only two male subjects completed the study, thus no statistical analysis was performed. Furthermore, the ambient temperature and relative humidity used during HA were not reported. Lastly, the degree of physiological acclimation that occurred in the subjects is unknown, since pre- and post-HA data for end-exercise core temperature and heart rate (HR) were not reported.

In light of the methodological concerns associated with these studies, it is debatable as to whether HA results in the peripheral modification of the human eccrine sweat gland. Therefore, the purpose of the current study was to determine if HA increases pharmacologically induced sweat production in human eccrine sweat glands.

2. Methods

The subjects for this study were 13 male volunteers. They had a mean ($\pm$SE) age, height, and weight of 22.5 ± 0.9 yr, 175.4 ± 2.1 cm, and 78.20 ± 2.01 kg, respectively. Prior to data collection, signed inform consent was obtained from each subject.

Each subject reported to the laboratory at approximately 7 a.m. for 8 consecutive days, excluding Sunday. A urine sample was immediately collected and measured for specific gravity. If need be, the subject consumed 200 ml of water every 15 min during seated rest until their urine specific gravity was $\leqslant 1.025$. Next, on days 1, 4, and 8, prior to that day's HA trial, peripheral sweat production was induced via pilocarpine iontophoresis on the

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proximal half of the flexor surface of both forearms. The reported value is the mean of both forearms. The iontophoresis current was fixed at 1.5 mA for 10 min, and was applied using a Wescor (Logan, UT) model 3700 inducer. Pilocarpine, an acetylcholine agonist, was delivered via reagent-impregnated (0.5% pilocarpine) solid agar gel discs (Pilogel, Wescor). Sweat was collected for 15 min immediately after iontophoresis using a Macroduct sweat collector (Wescor) according to the procedures outlined by Webster (1983). A different forearm site was used on each of the 3 measurement days to avoid any potential effects of desensitization of the glands from repeated pharmacological stimulation (Chen and Elizondo, 1974).

Each day during HA the subjects completed 2 h of exercise in an environmental chamber. The ambient temperature and relative humidity were controlled at 35 °C and 75%, respectively. This environment was selected since it is known (Armstrong and Maresh, 1991) that high humidity plays an important role in eliciting improvements in sweat gland function during HA. The exercise consisted of four 25-min intervals with 5 min of seated rest in the environmental chamber between each work interval.

The four exercise intervals included two bouts of walking on a motorized treadmill (3 mph, 3% grade) and two bouts of cycle ergometry at a power output of 60 W. The order of the first three exercise intervals was randomized; however the fourth and final exercise interval for all subjects, during which time the end-exercise HR and rectal temperature data were collected, was always walking on the treadmill. The alternating treadmill walking and cycle ergometry protocol was well tolerated by all the subjects and allowed for multiple subjects to be tested simultaneously. The oxygen uptake during the exercise intervals was approximately 1 l min^{-1}. During the exercise bouts core body temperature was measured each minute using a thermister (YSI 400 series) inserted 15 cm past the anal sphincter. Heart rate was measured each minute using a Polar monitor. Whole-body sweat rate, expressed in l m^2 h^{-1}, was calculated by measuring nude, dry pre- and post-exercise body weight, corrected for fluid intake and urine production, on a scale accurate to ±0.01 kg. DuBois body surface area was determined from height and weight.

A repeated measures ANOVA was used to analyze end-exercise HR, core temperature, WBSR, and pilocarpine-induced sweat rate. Significance was set at $p \leqslant 0.05$.

3. Results

The mean (±SE) rectal temperature during exercise was significantly reduced during the 8 days of HA. As shown in Fig. 1, it decreased from 38.9±0.2 °C on day 1 to 38.4±0.2 °C on day 8. In addition, as shown in Fig. 2, ending HR during exercise was also significantly reduced from 154±6 bpm on day 1 to 137±6 bpm on day 8 of HA. The magnitude of the decrease in rectal temperature and HR is consistent with the results of previous studies (Eichna et al., 1950; Pandolf et al., 1988; Strydom et al., 1966; Wyndham et al., 1968). Such reductions strongly suggest that the 8-day protocol used in the current study was successful in conferring HA in the subjects. The mean (±SE) WBSR and pilocarpine-induced sweat rate for the group are presented in Figs. 3 and 4, respectively. WBSR significantly increased from 0.55±0.06 to 0.66±0.05 l m^2 h^{-1}, or approximately 20%, as a result of HA. Again, these results are in agreement with previously published findings (Garden et al., 1966; Mitchell et al., 1976; Pandolf et al., 1988). The most important new finding of the current study was that HA produced a significant 63% increase in pilocarpine-induced sweat rate. Specifically, it increased from 0.64±0.06 mg cm^2 min^{-1} on day 1 to 1.04±0.11 mg cm^2 min^{-1} on day 8. Furthermore, mean pilocarpine-induced sweat rate significantly increased 42% following just 3 days of HA (Fig. 4).

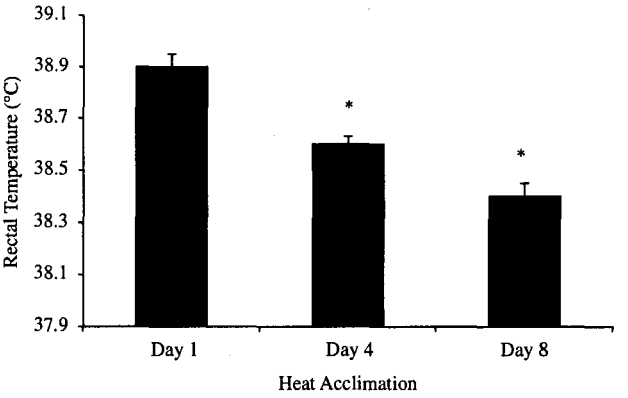

Fig. 1. Mean (±SE) end-exercise rectal temperature on days 1, 4, and 8 of heat acclimation. *Significantly ($p<0.05$) different than day 1 value.

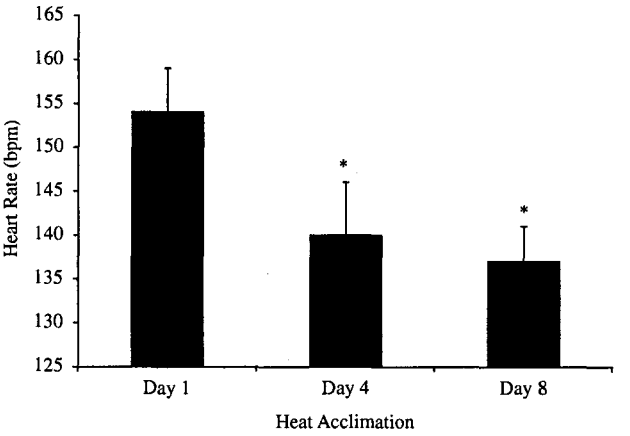

Fig. 2. Mean (±SE) end-exercise heart rate on days 1, 4, and 8 of heat acclimation. *Significantly ($p<0.05$) different than day 1 value.

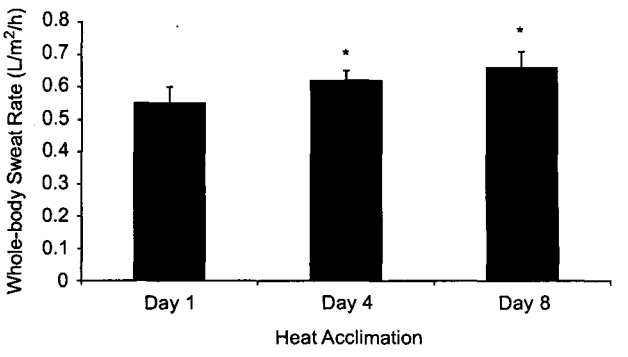

Fig. 3. Mean (±SE) whole-body sweat rate on days 1, 4, and 8 of heat acclimation. *Significantly ($p<0.05$) different than day 1 value.

4. Discussion

Four previous studies have attempted to determine if HA involves significant changes in thermoregulatory function at the

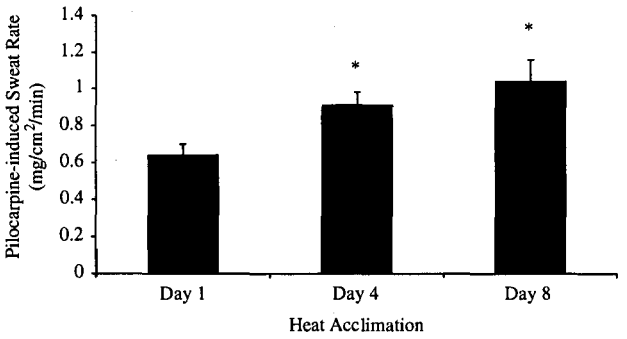

Fig. 4. Mean (±SE) pilocarpine-induced sweat rate on days 1, 4, and 8 of heat acclimation. *Significantly ($p<0.05$) different than day 1 value.

level of the eccrine sweat gland (Chen and Elizondo, 1974; Collins et al., 1966; Inoue et al., 1999; Sato et al., 1990). All of these studies, however, have methodological concerns, which make interpretation of the data difficult. Chen and Elizondo (1974) compared electrically stimulated forearm sweat production before and after 9 days of HA. The mean value increased 33% following HA; however, only four subjects participated in the study and no statistical analysis was performed on the data. Furthermore, the electrical current used to elicit sweat production was different for all four subjects and ranged between 1.0 and 1.6 mA. Lastly, although the subjects exercised for 90 min in a very hot (49 °C) environment, no physiological data were presented to confirm the degree of HA that occurred in the subjects.

Sato et al. (1990) were the first to provide experimental evidence that increased sweat gland function following HA was associated with morphological changes in the gland itself. They reported that both *in vitro* and *in vivo* methacholine-induced sweating was significantly increased following 9 months of HA in three Patas monkeys. The increased sweat capacity was accompanied by significant increases in the size of the eccrine glands. Unfortunately, due to concerns over the large dose of the tranquilizer needed to sedate the animals, the post-HA heat tolerance test could not be performed. Thus, they were not able to document that significant improvements in thermoregulatory function (e.g., decreased core temperature, decreased skin temperature, increased sweat rate, etc.) had occurred as a result of the 9 months of HA. Furthermore, after re-analyzing the pre- and post-HA *in vivo* methacholine-induced sweat rate data presented in Table 1 of the manuscript using a repeated measures ANOVA, we found that the 110% improvement was not significant ($p = 0.112$). Essentially, the large variability in the data, coupled with the small number ($n = 3$) of animals tested, made it difficult to find statistical significance.

Inoue et al. (1999) determined the methylcholine-induced sweat rate in young and old men following 8 days of HA. Heat acclimation produced significant reductions in heart rate and core temperature. Methylcholine-induced sweat rate measured on the chest, back, forearm, and thigh was significantly increased following HA. However, the photographic method used to estimate glandular sweat output does not provide an accurate quantitative value.

The results of the aforementioned studies (Chen and Elizondo, 1974; Collins et al., 1966; Inoue et al., 1999; Sato et al., 1990) suggest that HA alters sweat production at the glandular level; however, methodological concerns limit their applicability. The most important finding of the current study was that pilocarpine-induced sweat rate was significantly increased 63% as a result of HA. As identified by Sato and Sato (1993), improved peripheral sweat gland function following HA can be the result of (1) increased periglandular concentrations of acetylcholine, (2) increased cholinergic sensitivity of the eccrine sweat gland, or (3) increased glandular hypertrophy. There is no direct supportive evidence in the literature for the first possibility; however, previous studies (Okuda et al., 1980; Sato et al., 1990) do support the other two mechanisms. For example, Sato et al. (1990) found that long-term HA essentially doubled the size of the eccrine sweat glands of Patas monkeys. Furthermore, there was a significant linear relationship ($r = 0.87$) between sweat gland size and maximal *in vitro* sweat rate. In addition, Sato and Sato (1993) reported that human subjects who characterized themselves as "good sweaters" had significantly larger sweat glands than those who were non-athletic and considered themselves relatively poor sweaters. The larger sweat glands also had an increased cholinergic sensitivity as indicated by a higher pK_A during *in vitro* pharmacological stimulation. However, no data were presented that indicated the self-reported good sweaters were heat acclimated. Even with these limitations, the data suggest that HA results in sweat gland hypertrophy and increased cholinergic sensitivity. Certainly, further research examining the effect of HA on glandular hypertrophy in humans is warranted.

Additionally, the current study is the first in the literature to report that peripheral sweat gland function is significantly increased within the first 3 days of heat exposure (Fig. 4). Such a finding would agree with past studies which have shown that other known thermoregulatory parameters, such as WBSR, HR, and core temperature, can rapidly adapt during HA (Armstrong and Maresh, 1991; Strydom et al., 1966; Yamazaki and Hamasaki, 2003). For example, Strydom et al. (1966) found that following 3 days of HA the end-exercise rectal temperature and HR decreased by 0.5 °C and 10 bpm, respectively. Furthermore, during the same time frame, mean WBSR increased from 0.6 to 0.75 $l\,h^{-1}$, or 25%.

An interesting point raised by the data in the current study that warrants further discussion was the relative discrepancy in the percentage increase in WBSR vs. that seen in the pilocarpine-induced sweat rate. Specifically, following HA the mean WBSR increased 20% (Fig. 3) while the pilocarpine-induced sweat rate increased 63% (Fig. 4). Such a finding suggests that changes in WBSR may underestimate the true adaptation that occurred in sweat gland function as a result of HA. This could be due to the significantly lower end-exercise rectal temperature that occurred on day 8 vs. day 1. Specifically the mean rectal temperature on day 1 was 38.9 °C which produced a WBSR of 0.55 $l\,m^2\,h^{-1}$. On day 8 the mean rectal temperature was reduced to 38.4 °C, yet WBSR was still increased to 0.66 $l\,m^2\,h^{-1}$. It is well known that increases in core body temperature stimulate WBSR during exercise in the heat (Nadel et al., 1971; Saltin et al., 1970; Sawka et al., 1989). Since the central drive for sweat production (i.e., core temperature) is reduced at any given workload following HA, it should not be surprising that increases in WBSR underestimate the change in peripheral sweat gland function as measured by pharmacological stimulation. The current study is not the first to report such findings. Inoue et al. (1999) found that 8 days of HA did not change WBSR, yet methylcholine-induced sweat rate on the back, chest, forearm, and thigh were all significantly improved. Furthermore, when maximal WBSR is measured at the same core temperature, rather than at the same workload before and after HA, it has been shown to increase 60% (Wyndham, 1967). Likewise, Patterson et al. (2004) reported that 8 days of HA increased chest and forearm sweat rate approximately 65% when they used a controlled-hyperthermia acclimation technique, in which the workload was adjusted to achieve and maintain a target core temperature of 38.5 °C. These results agree in magnitude with the 63% increase in pilocarpine-induced sweat rate seen in the current study following HA (Fig. 4). Such findings suggest that

future studies should consider using a pharmacological-based sweat test to quantify improvements in sweat gland function following HA.

In summary, the current study strongly suggests that HA significantly improves sweat gland function via a peripheral mechanism. Furthermore, the improvement in sweat gland function is realized quite rapidly and can be seen with as little as 3 days of exercise in the heat.

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References

Armstrong, C.G., Kenney, W.L., 1993. Effects of age and acclimation on responses to passive heat exposure. J. Appl. Physiol. 75, 2162–2167.

Armstrong, L.E., Maresh, C.M., 1991. The induction and decay of heat acclimatisation in trained athletes. Sports Med. 12, 302–312.

Chen, W.Y., Elizondo, R.S., 1974. Peripheral modification of thermoregulatory function during heat acclimation. J. Appl. Physiol. 37, 367–373.

Collins, K.J., Crockford, G.W., Weiner, J.S., 1966. The local training effect of secretory activity on the response of eccrine sweat glands. J. Physiol. 184, 203–214.

Eichna, L.W., Park, C.R., Nelson, N., Horvath, S.M., Palmes, E.D., 1950. Thermal regulation during acclimatization in a hot, dry (desert type) environment. Am. J. Physiol. 163, 585–597.

Garden, J.W., Wilson, D., Rasch, P.J., 1966. Acclimatization of healthy young adult males to a hot-wet environment. J. Appl. Physiol. 21, 665–669.

Inoue, Y., Havenith, G., Kenney, W.L., Loomis, J.L., Buskirk, E.R., 1999. Exercise- and methylcholine-induced sweating responses in older and younger men: effect of heat acclimation and aerobic fitness. Int. J. Biometeorol. 42, 210–216.

Mitchell, D., Senay, L.C., Wyndham, C.H., Van Rensburg, A.J., Rogers, G.G., Strydom, N.B., 1976. Acclimatization in a hot, humid environment: energy exchange, body temperature, and sweating. J. Appl. Physiol. 40, 768–778.

Nadel, E.R., Mitchell, J.W., Saltin, B., Stolwijk, J.A.J., 1971. Peripheral modifications to the central drive for sweating. J. Appl. Physiol. 31, 828–833.

Nadel, E.R., Pandolf, K.B., Roberts, M.R., Stolwijk, J.A.J., 1974. Mechanism of thermal acclimation to exercise and heat. J. Appl. Physiol. 37, 515–520.

Okuda, N., Kanai, E., Watari, N., Ohara, K., 1980. Morphological changes of the eccrine sweat glands of Japanese monkey after heat acclimation: the mechanisms of peripheral adaptation. In: Szelenyi, Z., Szekely, M. (Eds.), Contributions to Thermal Physiology. Pergamon Press, New York, pp. 293–295.

Pandolf, K.B., Cadarette, B.S., Sawka, M.N., Young, A.J., Francesconi, R.P., Gonzalez, R.R., 1988. Thermoregulatory responses of middle-aged and young men during dry-heat acclimation. J. Appl. Physiol. 65, 65–71.

Patterson, M.J., Stocks, J.M., Taylor, N.A.S., 2004. Humid heat acclimation does not elicit a preferential sweat redistribution toward the limbs. Am. J. Physiol. Regul. Integr. Comp. Physiol. 286, R512–R518.

Roberts, M.F., Wenger, C.B., Stolwijk, J.A.J., Nadel, E.R., 1977. Skin blood flow and sweating changes following exercise training and heat acclimation. J. Appl. Physiol. 43, 133–137.

Saltin, B., Gagge, A.P., Stolwijk, J.A.J., 1970. Body temperatures and sweating during thermal transients caused by exercise. J. Appl. Physiol. 28, 318–327.

Sato, F., Owen, E., Matthes, R., Sato, K., Gisolfi, C.V., 1990. Functional and morphological changes in the eccrine sweat gland with heat acclimation. J. Appl. Physiol. 69, 232–236.

Sato, K., Sato, F., 1993. Individual variations in structure and function of human eccrine sweat gland. Am. J. Physiol. 245, R203–R208.

Strydom, N.B., Wyndham, C.H., Williams, C.G., Morrison, G.A., Bredel, G., Benade, A.J.S., Von Rahden, M., 1966. Acclimatization to humid heat and the role of physical conditioning. J. Appl. Physiol. 21, 636–642.

Sawka, M.N., Gonzalez, R.R., Young, A.J., Dennis, R.C., Valeri, C.R., Pandolf, K.B., 1989. Control of thermoregulatory sweating during exercise in the heat. Am. J. Physiol. Regul. Integr. Comp. Physiol. 257, R311–R316.

Webster, H.L., 1983. Laboratory diagnosis of cystic fibrosis. In: CRC Critical Reviews in Clinical Laboratory Sciences. CRC Press, Boca Raton, FL, pp. 313–338.

Wyndham, C.H., 1967. Effect of acclimatization on the sweat rate/rectal temperature relationship. J. Appl. Physiol. 22, 27–30.

Wyndham, C.H., Benade, A.J.A., Williams, C.G., Strydom, N.B., Goldin, A., Heyns, A.J.A., 1968. Changes in central circulation and body fluid spaces during acclimation to heat. J. Appl. Physiol. 25, 586–593.

Yamazaki, F., Hamasaki, K., 2003. Heat acclimation increases skin vasodilation and sweating but not cardiac baroreflex responses in heat-stressed humans. J. Appl. Physiol. 95, 1567–1574.

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14. ABSTRACT (maximum 200 words)

Background: This study was conducted to determine if humid heat acclimation improves thermoregulatory function at the level of eccrine sweat gland.
Methods: Thirteen male volunteers participated in this study, which consisted of 2 h of exercise in a thermal environment of 35˚C and 75% relative humidity for 8 consecutive days. All trials were randomized and consisted of four 25-min exercise intervals with 5 min of seated rest. The four exercise intervals consisted of two bouts of treadmill walking (3 mph, 3% grade) and two bouts of cycle ergometry (power output of 60 W). Heart rate and core temperature were measured each minute during the trials and whole-body sweat rate was calculated for the duration of the exposure. On days 1, 4, and 8 peripheral sweat production was induced via pilocarpine iontophoresis on the flexor surface of both forearms.
Results: Mean rectal temperature and heart rate were significantly reduced by 0.5^{o}C and 17 bpm, respectively, and whole-body sweat rate significantly increased by 20% during the 8-day heat acclimation protocol. Humid heat acclimation produced a significant 63% increase in pilocarpine-induced sweat rate.
Conclusion: The results strongly suggest that heat acclimation improves sweat gland function via a peripheral mechanism.

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